

PCT ENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 19 January 2001 (19.01.01)	
International application No. PCT/US00/15302	Applicant's or agent's file reference 37200-0001PC
International filing date (day/month/year) 01 June 2000 (01.06.00)	Priority date (day/month/year) 01 June 1999 (01.06.99)
Applicant HIRTZER, Pamela et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:28 November 2000 (28.11.00)☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Charlotte ENGER Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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REC'D 22 AUG 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 37200-0001PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/15302	International filing date (day/month/year) 01/06/2000	Priority date (day/month/year) 01/06/1999
International Patent Classification (IPC) or national classification and IPC A61K38/17		
Applicant NEURALAB, LTD. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 28/11/2000	Date of completion of this report 20.08.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Didelon, F Telephone No. +49 89 2399 7332 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15302

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-39 as originally filed

Claims, No.:

1-47 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/15302

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 39-42 (with respect to industrial applicability).

because:

☒ the said international application, or the said claims Nos. 39-42 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 5-38, 41-44, 47

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/15302

	No:	Claims	1-4, 39, 40, 45-46
Inventive step (IS)	Yes:	Claims	20-38, 43-44
	No:	Claims	1-19, 39-42, 45-47
Industrial applicability (IA)	Yes:	Claims	1-38, 43-47
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
se separate sheet

Comments on item III:

Claims 39-42 relate to methods of treatment of the human/animal body which is subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Comments on item V:

1. Reference is made to the following document:

D1: WO 91 16819 A (MOLECULAR RX) 14 November 1991 (1991-11-14)

2. The present application would not meet the requirements of Article 33(2) PCT because the subject-matter of claim 1-4, 39, 40, 45-46.

The present claims 1-4 relates to a "liquid solution" (see page 11, lines 7-8) of amyloid beta peptide which is in injectable form (see page 2, line 3) and administrable subcutaneously. It appears therefore that the amyloid beta (A β) being in solution, the pH of the solution has to be appropriate to allow solubilization of said peptide. In addition, the concentration of the peptide which is contemplated is 10-2 mg in 0.05 to 2 ml, which means that the solution can be at a concentration of up to 0.2 mg/ml, which falls within the scope of claims 1 (and 39).

Claims 1-4 therefore are not considered as novel (see also Guidelines of the PCT, Ch. IV, 7.5).

In addition, the solution containing amyloid beta when injected subcutaneously for treating or preventing Alzheimer's disease will obviously trigger an immune response. Thus, claims 39, 40, 45-46 do not either appear to be novel, because the claimed effect was already present in D1.

3. The specification of the form of the amyloid peptide and of the pH values to use are not considered sufficient to render claims 5-10 inventive, because the skilled person would use the same parameters of pH to achieve the solubilization, even if not

explicitly disclosed in D1. In addition, the specific A β 42 is the most common fragment known in the art, and would also be used preferentially. The buffers cited in claims 9-10 are mere alternative, with no particular technical effect. They cannot be considered as inventive.

It is also not clear which technical problem would solve claims 41, 42 and 47.

4. The lyophilized compositions (claims 11-19) prepared according to a standard process, i.e, by freezing a solution followed by a lyophilization, would not appear to be inventive with respect to the solid powder provided in D1 (see page 11, lines 7-8), for making a solid formulation for sublingual administration (see page 2, line 5). Since lyophilization will provide a highly soluble form of the medicament which will immediately be solubilized by the saliva and rapidly enter blood circulation, the skilled person in view of D1 would have used lyophilization to manufacture such sublingual tablets.
5. The suspensions (claims 20-30), the processes to prepare a solution (claims 31-38), compositions containing a suspension (claims 43-44) and the combination of the composition with various adjuvants are not disclosed nor contemplated in the prior art and would represent non-obvious alternatives to the solutions of D1.
6. For the assessment of the present claims 39-42 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Comments on item VIII:

1. Claims 1, 3, 11, 31 lack clarity in the sense of Article 6 PCT because they all relate to a composition having "a pH sufficient to solubilize said A β peptide". Such a wording appears a result to be achieved and misses the specific pH range which allows such a result.

Claim 31 similarly contains the step of dissolving into the solution "an amount of the A β peptide sufficient to achieve an immunogenic concentration for a mammal". Again said claim lacks the concentration range used to trigger said immunogenic response.

2. The relative term "about" should be avoided because when it relates to the pH values or concentration of the A β peptide, they bring uncertainty to the protection sought, especially because these two parameters are critical for the examination of novelty and inventive step of the present compositions or uses, when compared to D1.
3. The expression "invoking antibody response against an A β peptide in a mammal in need of such an antigenic response" found in claims 40 and 45 lacks clarity because it does not properly define the diseases sought to be treated by the use of the compositions of the application.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 37200-0001PC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 15302	International filing date (day/month/year) 01/06/2000	(Earliest) Priority Date (day/month/year) 01/06/1999
Applicant NEURALAB, LTD		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IS 00/15302

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K47/12 A61K47/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	W0 99 27944 A (ATHENA NEUROSCIENCES) 10 June 1999 (1999-06-10) cited in the application the whole document ---	1-47
A	W0 91 16819 A (MOLECULAR RX) 14 November 1991 (1991-11-14) the whole document -----	1-47



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

10 November 2000

Date of mailing of the international search report

16/11/2000

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Ventura Amat, A

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

P US 00/15302

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9927944 A	10-06-1999	BR 9815357 A EP 1033996 A NO 20002784 A AU 1706199 A	24-10-2000 13-09-2000 31-07-2000 16-06-1999
WO 9116819 A	14-11-1991	AT 153534 T CA 2081482 A DE 69126304 D DE 69126304 T EP 0526511 A JP 2980677 B JP 6502387 T US 5851996 A US 5753624 A	15-06-1997 28-10-1991 03-07-1997 04-09-1997 10-02-1993 22-11-1999 17-03-1994 22-12-1998 19-05-1998